UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA United States Environmental Protection Agency **Office of Pesticide Programs**

Antimicrobials Division (AD)

Friday, April 27, 2012

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 9402-RU
DP Barcode: D399987
Product Name: **HITMAN SPRAY**

From: Ian Blackwell, Biologist
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

Through: Karen Hicks, Team Leader
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

To: Marshall Swindell, PM 33/ *Demson Fuller*
Regulatory Management Branch
Antimicrobials Division (7510P)

Applicant: Kimberly-Clark Global Sales, LLC

FORMULATION FROM LABEL:

PC Code	Active Ingredient(s):	% by wt.
000595	Hydrogen peroxide	3.30
069208	Didecyldimethyl ammonium carbonate and Didecyldimethyl ammonium bicarbonate	1.38
	Other Ingredient(s):	95.32
	Total:	100.00

I BACKGROUND: Kimberly-Clark Global Sales, Inc., has submitted a set of seven acute toxicity studies to support the data requirements of their pending registration. Two of the seven studies are acute inhalation toxicity studies. In addition to the seven studies, there are two other documents with Master Record Identification Numbers (MRIDs) included in this submission.

1. 487484-05: "Acute Toxicity Discussion", Sally Hayes, Scientific & Regulatory Consultants, Inc. February 15, 2012.
2. 487484-06: "Hitman Spray Scientific Rationales to Support Acute Inhalation Toxicity", Kristini K. Miles, Ph.D. and Beth Mileson, Ph.D. Technology Sciences Group. 1/19/2012. This document addresses the rationale behind the registrants' providing two acute inhalation toxicity studies in one data submission.

II RECOMMENDATIONS:

1. The acute oral and dermal toxicity studies are acceptable.

2. The first acute inhalation toxicity study (MRID Number 487484-09) is acceptable. The second acute inhalation toxicity study (MRID Number 487484-10) is unacceptable. The problem with the second study is that more than one test dosage should have been tested. The second study only shows (implies, really) that the LC_{50} is less than 2.2 mg/L. The results of the two studies appear to contradict each other.

   A. MRID Number 487484-09: $LC_{50} > 2.0$ mg/L
   B. MRID Number 487484-10: $LC_{50} < 2.2$ mg/L

   The registrants assert that 487484-10 has a lower as it was tested using a whole body assay instead of a nose-only assay. CTT agrees with the registrant's rationale and assigns 9402-RU toxicity category IV for acute inhalation toxicity. When an acute inhalation toxicity study is conducted via whole body dosing, there can be absorption through the skin. There is also oral dosing of the test material in whole body studies as animals might lick themselves clean.

3. The primary eye irritation, primary skin irritation and dermal sensitization studies are acceptable.

The acute toxicity profile for File Symbol 9402-RU is currently:

Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	487484-07	IV	Acceptable
Acute Dermal Toxicity	487484-08	IV	Acceptable
Acute Inhalation Toxicity	487484-09	IV	Acceptable
	487484-10	?	Unacceptable
Primary Eye Irritation	487484-11	II	Acceptable
Primary Skin Irritation	487484-12	IV	Acceptable
Dermal Sensitization	487484-13	Nonsensitizer	Acceptable

III LABELING: (From the Label Review System)

PRECAUTIONARY STATEMENTS

SIGNAL WORD: WARNING

Hazards to Humans and Domestic Animals:

Restricted Use Pesticide due to toxicity categories. For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's certification.

Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse.

First Aid:

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1, 870.1100)

Up and Down Procedure

Product Manager: 33 **Reviewer:** I. Blackwell

MRID No.: 487484-07 **Study Completion Date:** 12/20/2011

Lab Study No.: MB 11-20288.01

Testing Laboratory: MB Research Laboratories

Authors: Blair Yasso, B.S., Study Director

Quality Assurance (40 CFR §160.12): Included

Test Material: C2010-1673 Hitman disinfectant, Lot #SA1255BLB, Lot 4. "clear, colorless liquid"

Species: Sprague Dawley rat

Weight: 190-214 g **Age:** ~ 10 weeks

Source: SAGE Labs

Conclusion:

1. LD_{50} (mg/kg):

Males= Not tested

Females> 5,000 mg/kg

Combined= ---

2. The estimated LD_{50} is greater than 5,000 mg/kg body weight.

3. Tox. Category: IV **Classification:** Acceptable

Procedure (Deviations from §81-1): None

Results:

Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
5,000	---	0/3	---

Observations: Anogenital soiling. No other abnormal signs were observed.

Gross Necropsy: The lab reported no observable abnormalities.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: 33 **Reviewer:** I. Blackwell
MRID No.: 487484-08 **Study Completion Date:** 1/3/2012
Lab Study No.: MB 11-20288.02

Testing Laboratory: MB Research Laboratories
Author: Laura J. DiDonato, B.S., Study Director
Quality Assurance (40 CFR §160.12): Included

Test Material: C2010-1673 Hitman disinfectant, Lot #SA1255BLB, Lot 4. "clear, colorless liquid"

Species: New Zealand White Albino rabbit
Weight: Males= 2.7-3.1 kg **Age:** ~ 25 weeks
Females= 2.8-3.0 kg
Source: Covance Research Products

Summary:

1. **LD_{50} (mg/kg):**
   Males > 5,000 mg/kg b.w.
   Females > 5,000 mg/kg b.w.
   Combined

2. **The estimated LD_{50} is**

3. **Tox. Category:** **Classification:**

Procedure (Deviation From §81-2): None

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
5,000	0/5	0/5	0/10

Observations: Lack of feces from one female.

Gross Necropsy Findings: The lab reported no observable abnormalities.

DATA REVIEW FOR ACUTE INHALATION TOXICITY (§81-3, 870.1300)

Product Manager: 33 **Reviewer**: I. Blackwell
MRID No.: 487484-09 **Study Completion Date**: 1/28/2012
Lab Study No.:

Testing Laboratory: IIT Research Institute (IITRI)
Author: Dennis Sullivan, M.S., D.A.B.T.

Quality Assurance (40 CFR §160.12): Included

Test Material: C2010-1673 Hitman disinfectant ()Lot #SA1255BLB, Lot 4). "clear, colorless liquid"

Concentration: nose-only exposure. Gravimetric= 2 mg/L. Nominal= 7.22 mg/L

Species: Sprague-Dawley derived rats
Weight: Males= 192-199 g Females= 159-174 g
Age: 49 days
Source: Charles River Laboratories

Summary:

1. **LC_{50} (mg/L)** **Males** > 2.0 mg/L
   Females > 2.0 mg/L
   Combined > 2.0 mg/L
2. **The estimated LC_{50} is greater than 2.0 mg/L.**
3. **MMAD:** 1.86 **µm**
4. **Toxicity Category:** IV **Classification:** Acceptable

Procedure (Deviation From §81-3): None

Results:

Reported Mortality

Exposure Concentration	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
2 mg/L	0/5	0/5	0/10

Chamber Atmosphere			
Dose Level	MMAD	GSD	particles < μm
2.03 mg/L	1.86 μm	2.45 μm	

Chamber Environment	
Chamber Volume	Not reported
Airflow	28.12 LPM
Temperature	22.8° C
Relative Humidity	99.9%
Oxygen	20.8

Clinical Observations: Hypoactivity, salivation, labored breathing, rales, rough coat, redness on muzzle.

Gross Necropsy Findings: The laboratory reported no gross lesions in any animal at terminal necropsy.

DATA REVIEW FOR ACUTE INHALATION TOXICITY (§81-3, 870.1300)

Product Manager: 33 **Reviewer:** I. Blackwell
MRID No.: 487484-10 **Study Completion Date:** 2/17/2012
Lab Study No.: MB 11-20288.05

Testing Laboratory: MB Research Laboratories
Author: Blair Yasso, B.S., Study Director

Quality Assurance (40 CFR §160.12): Acceptable

Test Material: C2010-1673 Hitman disinfectant, Lot #SA1255BLB, Lot 4. "clear, colorless liquid"
Concentration: Gravimetric= 2.2 mg/L, Nominal concentration= 40.48 mg/L

Species: Sprague-Dawley rats
Weight: Males= 292-370 g Females= 215-251 g
Age: 10 weeks
Source: SAGE Labs

Summary:

1. **LC_{50} (mg/L)** **Males=** **Females=** **Combined=**
2. **The estimated LC_{50} is**
3. **MMAD:** **µm**
4. **Toxicity Category:** **Classification:** Unacceptable

Procedure (Deviation From §81-3):

- Further dosages needed to be tested.
- The study did not determine an LC_{50}.

Results:

Reported Mortality

Exposure Concentration	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
2.20 mg/L	4/5	3/5	7/10

Chamber Atmosphere			
Dose Level	MMAD	GSD	particles < 4.7µm
2.20	1.70 µm	4.47 µm	67%

Chamber Environment	
Chamber Volume	100 liter
Airflow	20 LPM
Temperature	19-22° C
Relative Humidity	34-38%

Clinical Observations: Emaciation, chromodacryorrhea, chromorhinorrhea, muzzle stained red, anogenital area wet, dyspnea, fur coated with test article.

Gross Necropsy Findings: Liver darker than normal with pale areas, adrenal gland enlarged. Stomach red, distended with fluid and/or distended with gas. Intestines with red or yellow areas, or, distended with gas.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: 33 **Reviewer:** I. Blackwell
MRID No.: 487484-11 **Study Completion Date:** 1/2/2012
Lab Study No.: MB 11-20288.04

Testing Laboratory: MB Research Laboratories
Author(s): Debra A. Hall, LATG, Study Director

Quality Assurance (40 CFR §160.12): Included

Test Material: C2010-1673 Hitman disinfectant, Lot #SA1255BLB, Lot 4. "clear, colorless liquid"
Dosage: 0.1 mL

Species: New Zealand White Albino rabbit **Sex:** 2 males + 1 female
Weight: 2.9-3.0 kg **Age:** 24 weeks
Source: Covance Research Products, Inc.

Summary:

1. **Toxicity Category:** II

2. **Classification:** Acceptable

Procedure (Deviations From §81-4):

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Corneal Opacity	0/3	0/3	1/3	1/3	---	1/3	0/3	0/3
Iritis	0/3	1/3	1/3	1/3	---	0/3	0/3	0/3
Conjunctivae								
Redness	1/3	3/3	3/3	3/3	---	1/3	0/3	0/3
Chemosis	3/3	3/3	2/3	2/3	---	1/3	0/3	0/3
Discharge	3/3	3/3	2/3	2/3	---	0/3	0/3	0/3

- - - = no observations at this point

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 33 **Reviewer**: I. Blackwell
MRID No.: 487484-12 **Study Completion Date**: 2/16/2012
Lab Study No.: MB 11-20288.03

Testing Laboratory: MB Research Laboratories
Study Director: Laura J. DiDonato, B.S., Study Director

Quality Assurance (40 CFR §160.12): Included

Test Material: C2010-1673 Hitman disinfectant, Lot #SA1255BLB, Lot 4. "clear, colorless liquid"
Dosage: 0.5 mL

Species: New Zealand White albino rabbits
Weight: 2.8-3.0 kg **Age**: 25 weeks
Source: Covance Research Products

Summary:

1. **Toxicity Category**: IV

2. **Classification**: Acceptable

Procedure (Deviations From §81-5):

Results: The lab reported no erythema, but, very slight edema in 1/3 test material-treated subjects during the study. The study was terminated after 72 hours.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: 33 **Reviewer**: I. Blackwell
MRID No.: 487484-13 **Study Completion Date**: 1/2/2012
Lab Study No.: MB 11-20288.06

Testing Laboratory: MB Research Laboratories
Author: Debra A. Hall, LATG, Study Director

Quality Assurance (40 CFR §160.12): Included

Test Material: C2010-1673 Hitman disinfectant, Lot #SA1255BLB, Lot 4. "clear, colorless liquid"

Positive Control Material: α-Hexyl cinnamaldehyde (HCA)

Species: Hartley albino guinea pigs
Weight: Males= 292-361 g **Age**: 3 weeks
Females= 281-354 g
Source: Elm Hill Breeding Labs, Inc.

Method: Buehler Method

Summary:

1. **This Product is not a dermal sensitizer.**

2. **Classification**: Acceptable

Procedure (Deviation From §81-6):

Procedure:
Induction Group 1: Ten males and ten females were treated with 0.4 mL of 100% test material. The dose of test material using a 25 mm HillTop Chamber. After 6 hours, the test material was removed. This treatment was repeated once per week on the same day each week for three weeks. Fourteen days after the induction exposure, the test material-treated and naïve control animals were challenged using the same 0.4 mL at 25% test material at dosing procedure as in the induction phase in a naïve treatment site.

Results: Twenty-four hours after induction treatment #1, erythema was absent to moderate. Twenty-four hours after induction treatment #2, erythema to absent to strong with eschar. Twenty-four hours after induction treatment #3, erythema to absent to strong with eschar.

Twenty-hours after challenge, 1/10 displayed very slight confluent erythema and 1/10 very slight patchy erythema.